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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,068	09/20/2001	Hazire Oya Alpar	41577/263898	6302

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EXAMINER	
FIELD, TAMMY K	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/937,068	ALPAR ET AL.	
	Examiner	Art Unit	
	Tammy K. Field	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *14-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Election/Restrictions

1. Applicant timely traversed the restriction (election) requirement of Group I (Claims 1-13) and the elected species of "positively charged cationic pluronics" (Species C) received in the Office October 29, 2003. The traversal is on the ground(s) that all the Species in Claim 1 describes a group of compounds that had not previously been recognized as adjuvants and they are able to enhance the effect of biological materials. This is not found persuasive because as cited in the Election/Restriction Office action, the art of Duncan, J.D., *et al.* (International Application WO 94/20070 published September 15, 1994) teach a four component composition comprising: (i) a biologically active agent, *e.g.* immunogens or antigens at page 4, paragraph 1-page 5, paragraph 1, (ii) an adjuvant chemical, *e.g.* polyarnithine or vitamin A at page 9, paragraph 1-page 10, paragraph 1, and (iii) a pharmaceutically acceptable carrier, *e.g.* mucoadhesive at page 6, paragraph 1 were recognized in the prior art as adjuvants.

In response to Applicants' traversal for determining lack of unity by the reference, PCT Publication WO 94/20070, in that the reference does not render the present invention obvious or anticipated because it is a speculative disclosure, is noted, but not found persuasive as this published reference is available to the public and one skilled in the art may utilize the information disclosed therein. Additionally, Applicants submission that vitamin A is not a water soluble vitamin is noted. The claims recite in Claim 1(ii), c) a water soluble vitamin or vitamin derivative (emphasis added) and respectfully submit vitamin A is a vitamin derivative.

The requirement is still deemed proper and is therefore made **FINAL**.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

2. Claims 14-25 have been withdrawn from consideration.

3. The Invention of Group I (Claims 1-13) that read on the elected species of positively charged cationic pluronics are presently under examination.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/937,068, filed on September 20, 2001.

Information Disclosure Statement

5. The information disclosure statement filed on December 17, 2001 has been considered. An initialed copy is enclosed.

Claim Objections

6. The following Claims are objected to because of the following informalities:

a. Claim 11 – "carrier" needs to recite "carrier (iii)".

b. Claims 3 and 4 – "wherein the said" should be either "wherein the" or "wherein said".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claim s 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Claims encompass a pharmaceutical composition comprising a biologically active agent, adjuvant chemical of positively charged cationic pluronics, and carrier or diluent capable of generating a protective immune response. Further claims encompass a microsphere carrier for mucosal surface or parenteral administration.

The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims and bounds of the claimed subject matter. The claims are indefinite in the recitation in Claims 1 and 2; "agent ... is capable", Claim 12: "A composition ... adapted for administration... suitable for parenteral administration", Claim 13; and "composition according to claim 2 which further comprises a further adjuvant" because it is unclear from the specification what applicant intends. How does Applicant determine if an agent is "capable"? What does Applicant intend by "adapted" and "suitable" for administration? Does Applicant intend one or two adjuvants in the composition?

For purposes of examination, pharmaceutical compositions containing one and/or two adjuvants will be considered.

Regarding claim 4, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Clarification is required in order to overcome this rejection.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-9 and 11-13 rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Duncan, D. *et al.* (International Application WO 94/20070 published September 15, 1994).

Duncan, D. *et al.* teach a four component composition comprising: (i) a biologically active agent, *i.e.* immunogens or antigens at page 4, paragraph 1- page 5, paragraph 1, (ii) an adjuvant chemical having adjuvant properties, *i.e.* Pluronic® block copolymers, polycations,

such as DEAE-4 dextran and polyarnithine at page 9, paragraph 1- page 10, paragraph 1, and (iii) an acceptable carrier, *i.e.* mucoadhesive at page 6, paragraph 1. Also pertaining to the applicant's instant claim 1 (iii), Duncan, J.D., *et al.* further teach the immunogen, mucoadhesive and adjuvant combined with a pharmaceutically acceptable liquid vehicle, *i.e.* water or buffered saline at page 11, paragraph 1. Duncan, J.D., *et al.* also teaches that an enhancement in immune response is observed when the adjuvant is combined with the immunogen and mucoadhesive, (iv) *i.e.* delivery system or vaccine for oral administration, at page 10, paragraph 2 - page 11, paragraph 3. Duncan, J.D., *et al.* also teach antigens incorporated into or attached to polymeric microparticles, nanoparticles, or liposomes are frequently more immunogenic at page 2.

The products of the prior art references of Duncan, J.D., *et al.* are in an analogous field of endeavor and appear to be the same as the pharmaceutical composition claimed by the applicant because they appear to possess the same or similar functional characteristics, i.e. microsphere prepared using a high molecular weight polymer of 100Kda or more and a composition wherein the ratio of the chemical (ii), *i.e.* Pluronic® block copolymers, polycations, such as DEAE-4 dextran and polyarnithine to the carrier is from 99.1 to 9.1 w/w (instant Claims 8, 9, and 11). The production of a composition by a particular process does not impart novelty to a composition when the same composition is taught by the prior art. This is particularly true when the properties of the composition are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 29222-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

It would have been prima facie obvious to one having ordinary skill in this art at the time the invention was made to make a pharmaceutical composition comprising a biologically active

agent, adjuvant chemical of positively charged cationic pluronics, and carrier or diluent capable of generating a protective immune response in a microsphere carrier for mucosal surface or parenteral administration. The motivation for doing what Applicants has claimed is present in the pharmaceutical composition of the prior for enhancing the immune response against disease as taught by Duncan, J.D., *et al.*

Thus, Duncan, D. *et al.* anticipates or, in the alternative as obvious over the instantly claimed invention.

9. Since the office does not have the facilities for examining and comparing applicants' pharmaceutical composition with the compositions disclosed in the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed pharmaceutical composition and the pharmaceutical composition of the prior art (*i.e.* that the pharmaceutical composition of the prior art does not possess the same material structural and functional characteristics of the claimed pharmaceutical composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald *et al.*, 205 USPQ 594.

Status of the Claims

10. No claims allowed.

Conclusion

11. The prior art of record and not relied upon is considered pertinent to applicant's disclosure.

a. Alpar *et al.* US Pregrant Publication 2003/0171258, Published September 11, 2003. Particle based vaccine composition.

b. Park *et al.* US Patent 6,267,987 B1, Published July 31, 2001. Positively charged poly[alpha(omega-aminoalkyl) glycolic acid] for the delivery of a bioactive agent via tissue and cellular uptake.

c. Kotze, A.F. *et al.* N-trimethyl chitosan chloride as a potential absorption enhancer across mucosal surfaces: *in vitro* evaluation in intestinal epithelial cells (Caco-2). Pharmaceutical Research 14(9): 1197-1202.

d. Eyles, J.E. et al. Intra nasal administration of poly-lactic acid microsphere co-encapsulated Yersinia pestis subunits confers protection from pneumonic plague in the mouse. 1998. Vaccine:16(7): 698-707.

e. Griffin, K.F. et al. Immune responses to V antigen of Yersinia pestis co-encapulated with IFN-gamma: effect of dose and formulation. 1998. Vaccine 16(5): 517-521.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tammy K. Field whose telephone number is (703) 305-4447. The examiner can normally be reached on Monday-Friday from 7am-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909.

Papers relating to this application may be submitted to Technology Center 1600 Group 1640 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Tammy K. Field
December 11, 2003

NITA MINNIFIELD
PRIMARY EXAMINER
12/11/03
AU 1645